

Bayer Corporation Comments
Guidance for Industry: 21 CFR Part 11; Electronic Records; Electronic Signatures Timestamps
Draft Guidance – February 2002
Docket No. 00D-1542

Page Number of PDF Guidance Document	Section Title	Comments/Recommendations for Revision
Pages 3-4	4. Regulatory Requirements; What Does Part 11 Require?	Document states, "To satisfy this requirement persons must, among other things, employ procedures and controls that include the use of computer generated time stamps." The wording "among other things" is ambiguous. Suggested wording to replace "among other things" is "in addition to other procedures and controls..." The full sentence with the replacement wording would read, "To satisfy this requirement persons must, in addition to other procedures and controls, employ procedures and controls that include the use of computer generated time stamps."
Page 4	5.1 Time Stamp Accuracy	Document states, "Persons must use procedures and controls for time stamps under Part 11 (as described above), designed to ensure, among other things, the authenticity and integrity of electronic records." The wording "among other things" is ambiguous.
Page 5	5.1.1 Synchronization	The document states, "Computer clocks should be set correctly and continue to be set correctly." We recommend the following language, "Clocks of computers subject to 21 CFR Part 11 should be set correctly and continue to be set correctly."

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Page 5	5.1.1 Synchronization	The document states, "For example, computers on a network should..." This is a recommendation for implementation and should instead read, "For example, computers on a network could..." This applies to the rest of the paragraph.
Page 5	5.1.1 Synchronization	The document states, "For example, computers on a network should automatically synchronize their clocks with that of a designated network computer..." The document further implies that each company should have a standard clock that is used to set server clocks and that this clock is also maintained and kept secure. It is technically very difficult for all computers in a network to be perfectly synchronized. Even the "events" on the network are not synchronized (in other words with multiple nodes, the only sequence of events that can be determined are local not network transactions). There should be a margin for error and error tolerance should be defined locally. A more practical approach to "synchronization" is that all related events or signatures should be time sequenced (and possibly indexed) by the application that is relevant to those events or signatures. If transactions occur between different systems, these transactions might also be sequenced so that the order in which the events occurred takes precedence over the absolute time at a location (or Universal Coordinated Time). This eliminates problems with clock synchronization, daylight savings time and local time because all events, signatures, and records are sequenced relative to their occurrence.

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Page 5	5.1.1 Synchronization	The document states, "Computers not connected to a network should have their clocks synchronized to a recognized standard clock and should be periodically verified against the standard clock." This requirement may be difficult to implement. Clocks on laptops should be synchronized upon connection to the network. In general, there is no easy solution for stand-alone workstations that are common throughout industry manufacturing and laboratory environments.
Pages 5-6	5.2 Systems Clock Security	Although modern operating systems allow for security settings to prevent users from changing system clocks (even on laptops), it is difficult to detect inappropriate changes to the system clock because there is no event logging or audit trail that automatically records changes to the system clock. We propose that whenever technically feasible, server created time stamps be used. This solves some of the problems associated with time zone information since the time stamp always refers to the server's time zone setting and is therefore unambiguous. Time stamps created by software running on the client computer should only be acceptable if the users are not able to change the clock setting by appropriate operating system security settings. We further recommend that this issue also be addressed through training and procedures as opposed to requiring additional technical controls.

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Pages 5-6	5.2 Systems Clock Security	The guidance does not address Contract Research Organizations (CROs). A phrase like, "A company should take the position that it is authorized to conduct the same degree of checks of computer clocks for external persons or organizations as for employees" should be added at the end of the paragraph.
Pages 5-6	5.2 Systems Clock Security	The requirement to "periodically conduct unannounced checks of computer clocks to detect and deter unauthorized clock changes" seems extraordinary. Actual implementation is not practical and the benefit does not appear to be greater than the costs of implementation. This issue should be addressed through training and procedures. Some level of trust must exist between the organization and employees or all activities must be suspect.
Pages 5-6	5.2 Systems Clock Security	The statement, "Persons responsible for system security should periodically conduct unannounced checks of computer clocks to detect and deter unauthorized clock changes," is too specific with respect to who should do the checks. Individuals other than those responsible for system security could just as effectively perform these checks (e.g., Quality Assurance or system administrators).
Pages 5-6	5.2 Systems Clock Security	Periodic checks of client computers should only be required if client created time stamps are in use, the users may change the system clock, and/or there is no automatic synchronization to a server based master clock.

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Page 6-7	5.3 Time Zones	Prioritization as to whether or not to implement the time zone as part of the time stamp should be given to global systems that are accessed by users in different time zones. For local systems, inclusion of time zones as part of the time stamp should be considered based on a risk assessment of the system.
Pages 6-7	5.3 Time Zones	If time zone information is relevant for a system the exact behavior and treatment of this information when storing and displaying times stamps has to be defined and implemented very carefully. Numerous bugs and strange behavior of operating systems as well as commercial software is known when time stamp information is stored and/or displayed with different time zone or daylight saving settings.
Pages 6-7	5.3 Time Zones	Although it may be logical in some circumstances to include the time zone reference as part of the time stamp, implementation of this requirement would require providing a greater level of detail than that required of the predicate paper record. It should be open to the company how to implement a consistent time zone reference. The sentence, "The time zone reference should be part of the time stamp itself..." should be revised to read, "It is FDA's recommendation to implement the time zone reference as part of the time stamp..."

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Page 8	5.4 Expression of Date and Time	Similar to our comments on times zones expressions of date and time should be defined at the local level for local systems. Moreover, even for global systems it is only of relevance if transactions or concurrent data entries are performed across multiple time zones.
Page 8	5.5 Precision of Date and Time Expressions	This section states that manufacturing systems are excluded from the scope of the guidance document. This is in conflict with section 2.1 of the guidance document, which includes manufacturing systems.
Page 8	5.5 Precision of Date and Time Expressions	The statement, "Audit Trail and signature time stamps should be precise to the hour and minute," places a higher demand than the requirements for handwritten signatures. The sentence should be revised to read, "Audit trail time stamps should be precise to the hour and minute, signatures to the day..."
Page 9	6. Other Uses of Time Stamps in Electronic Recordkeeping	This paragraph is not necessary. The guidance document should only include required information.

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Page 9	6. Other Uses of Time Stamps in Electronic Recordkeeping	In response to second bullet point, ensuring proper sequencing of events should not be done “post facto.” If the electronic system is used as a paper record, the only thing it can capture is the order of entry; not the order events being attested to occur (this is dependent on the person entering the information). If the system enforces an order of entry, then this will be the only way data is entered whether or not the physical events recorded occurred in that order. The computer can only be validated to record the correct sequence of events that it can “see” and even this may be subject to polling issues in the minute range. Applying reliable timestamps to each event in a sequence of human actions can not prove that these happened in chronological order.

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